A new immunodeficient pigmented retinal degenerate rat strain to study transplantation of human cells without immunosuppression.

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Public Summary:
PURPOSE: The goal of this study was to develop an immunodeficient rat model of retinal degeneration (RD nude rats) that will not reject transplanted human cells. METHODS: SD-Tg(S334ter)3Lav females homozygous for a mutated mouse rhodopsin transgene were mated with NTac:NIH-Whn (NIH nude) males homozygous for the Foxn1 rnu allele. Through selective breeding, a new stock, SD-Foxn1 Tg(S334ter)3Lav (RD nude) was generated such that all animals were homozygous for the Foxn1 rnu allele and either homo- or hemizygous for the S334ter transgene. PCR-based assays for both the Foxn1 rnu mutation and the S334ter transgene were developed for accurate genotyping. Immunodeficiency was tested by transplanting sheets of hESC-derived neural progenitor cells to the subretinal space of RD nude rats, and, as a control, NIH nude rats. Rats were killed between 8 and 184 days after surgery, and eye sections were analyzed for human, neuronal, and glial markers. RESULTS: After transplantation to RD nude and to NIH nude rats, hESC-derived neural progenitor cells differentiated to neuronal and glial cells, and migrated extensively from the transplant sheets throughout the host retina. Migration was more extensive in RD nude than in NIH nude rats. Already 8 days after transplantation, donor neuronal processes were found in the host inner plexiform layer. In addition, host glial cells extended processes into the transplants. The host retina showed the same photoreceptor degeneration pattern as in the immunocompetent SD-Tg(S334ter)3Lav rats. Recipients survived well after surgery. CONCLUSIONS: This new rat model is useful for testing the effect of human cell transplantation on the restoration of vision without interference of immunosuppression.

Scientific Abstract:
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